REMARKS

Applicants would like to thank the Examiner for her time and helpful comments during the informal telephone interview of January 17, 2002.

Cancellation of Non-elected claims

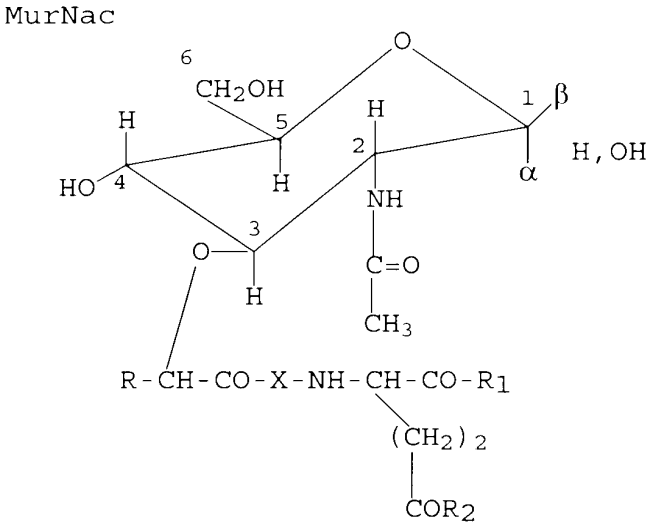
The Examiner indicates that Applicants should cancel non-elected claims 27 and 35-40. Applicants respectfully note that the Examiner's designation of withdrawn claims appears to be in error. Applicants elected the species of murabutide in the response of January 8, 1999, leading to the withdrawal of claim 27 and further elected methods of inhibiting the replication of acquired immune deficiency in the response of November 5, 1999, leading to the withdrawal of claim 36. Claims 35 and 37-40 are drawn to embodiments of the elected invention, therefore should not be withdrawn. Review of the designation of the withdrawn claims by the Examiner is requested. Claims 27 and 36 have been duly cancelled.

Rejections under 35 U.S.C. §102(b)

1) Schreck et al. - Claims 25, 26, 28-30 and 34 have been rejected under 35 U.S.C. §102(b) as being anticipated by Schreck

et al. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The present invention, as encompassed by independent claim 25, is drawn to a process for inhibiting the replication of acquired immunodeficiency retroviruses by administering a muramyl peptide of the following formula:



wherein the amount of muramyl peptide used also causes 100% inhibition of the replication of the retroviruses in primary monocyte cultures of the host. For a reference, "to anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently." Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 34 U.S.P.Q.2d 1565 (Fed. Cir. 1995).

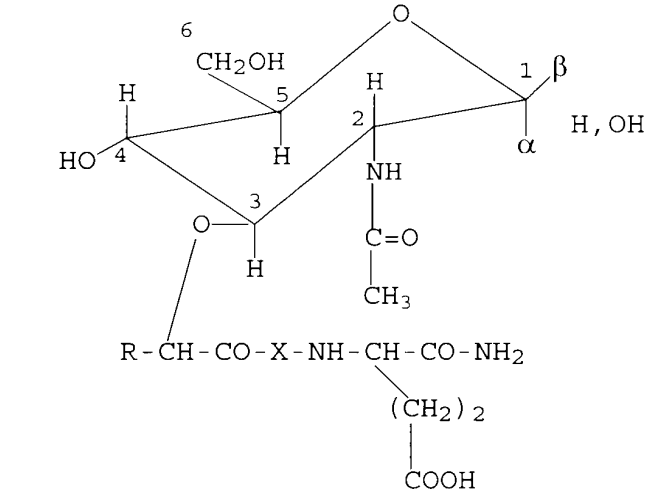
Schreck et al. "examined a battery of synthetic immunostimulants of the muramyl peptide family for their ability to activate NF-κB in different human and mouse cell lines" and "demonstrate selective activation of NF-κB in different cell lines...." See "SUMMARY". As further stated in the final sentence of Schreck et al., the studies of the reference pertained to the "screening of potential adjuvants for human use...." There is no disclosure or suggestion in Schreck et al. of using muramyl peptides to inhibit retrovirus replication *in vitro* or in *vivo*.

The disclosure of Schreck et al. pertains to assessing the activation of NF-κB by various adjuvants. However, the tested adjuvants of Schreck et al. are never exposed to HIV virus. For example, the experiments of Figures 1, 2 and 3 tested the ability of muramyl peptides and SDZ MRL 953 to activate NF-κB in Jurkat T cells, the monocyte macrophage line Mono-Mac-6, and the mouse pre-B cells 70Z/3 cells. The experiments of Figure 4 tested the effects of dithiocarbamates on the ability of muroctasin to activate NF-κB in Mono-Mac-6 cells and the experiments of Figure 5 considered the induction of IL-8 mRNA in Mono-Mac-6 cells. None the experiments of Schreck et al. used HIV and none of the cells of the experiments were infected with HIV. As such, it is not possible for Schreck et al. to achieve the presently claimed method of inhibiting

retroviruses. As such, the present invention is not anticipated by Schreck et al. and withdrawal of the rejection is respectfully requested.

2) Masihi et al. - Claims 25, 26, 28-30 and 34 have been rejected under 35 U.S.C. §102(b) as being anticipated by Masihi et al. Masihi et al. discloses the ability of the muramyl peptide MDP to inhibit HIV *in vitro*. MDP has the following chemical structure.

MDP



Thus with MDP R_1 is NH_2 and R_2 is "OH".

R_1 and R_2 of the compounds used in the method of claim 25 of the present invention are as follows: R_1 = $O(CH_2)_xH$, wherein x is 1, 2, 3 or 4 and ; R_2 = an amino group or $O(CH_2)_xH$, wherein x is 1,

2, 3 or 4. Thus, the present invention does not encompass the use of MDP. As such, the present invention is not anticipated by Masihi et al. and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §103

Claims 31-33 have been rejected as being obvious over Masihi et al. The Examiner asserts that Masihi et al. teach the use of MDP as an adjuvant in treating AIDS and the use of recombinant GM-CSF with zidovudine. The Examiner asserts that it would be obvious to combine MDP with another peptide such as cytokine or GM-CSF or protease inhibitor to achieve the invention of claims 31-33. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

To establish a *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP §2142. In addition, if a reference needs to be modified to achieve the claimed invention "there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion." Sibia Neurosciences Inc. v. Cadus Pharmaceutical Corp. 55 USPQ2d 1927 (Fed. Cir. 2000). As discussed

above with regard to the rejection under 35 U.S.C. §102(b), Masihi et al. discloses the use of MDP as an adjuvant. However, the present compositions do not encompass MDP peptide. To achieve the invention of claims 31 to 33, one skilled in the art would not only have to include a cytokine, GM-CSF or protease inhibitor, but would also be required to modify the muramyl peptide, which is the primary active component responsible for inhibition of viral replication. In addition, one skilled in the art would need to modify the muramyl peptide used so as to meet the additional limitation that 100% inhibition of viral replication in monocytes is achieved *in vivo*. The Examiner has provided no motivation for modifying MDP of the compositions of Masihi et al. to the muramyl peptides used in the method of the present invention. Nor can any such motivation be found in the reference. As such, the invention of claims 31-33 is not obvious over Masihi et al. and withdrawal of the rejection is respectfully requested.

Applicants note that the present invention further possesses unexpected results over the disclosure of Masihi et al. Masihi et al. achieve less than 50% inhibition of viral replication with a monocyte cell line *in vitro*. The present invention, on the other hand, achieves 100% inhibition of viral replication with monocytes *in vitro*. There is no suggestion or disclosure of this high level

of inhibition from Masihi et al. Nor would one skilled in the art have expected to achieve 100% inhibition, since an extremely high dose of MDP, 1000μg, achieved less than 50% inhibition with Masihi et al. As such, the present invention of claims 31-33 is not obvious over Masihi et al. and withdrawal of the rejection is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D. (Reg. No. 40,069) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $200.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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2121-0128P

(Rev. 02/12/01)